2	CAS No.: 96-45-7	Substance: 2-Imidazolidinethione

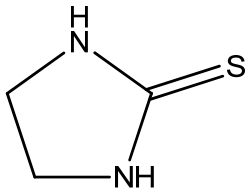
Chemical Substances Control Law Reference No.: 5-423

PRTR Law Cabinet Order No.: 1-42

Molecular Formula: $C_3H_6N_2S$

Molecular Weight: 102.16

Structural Formula:



1.**General information**

The aqueous solubility of this substance is 2.74×10^4 mg/L (20°C), the partition coefficient (1-octanol/water) (log K_{ow}) is –0.66, and the vapor pressure is 2.0×10^{-6} mmHg (=2.7×10^{-4} Pa) (25°C, extrapolated value). The biodegradability (aerobic degradation) is characterized by a BOD degradation rate of 0%, and bioaccumulation is thought to be nonexistent or low. In addition, the substance is extremely stable towards hydrolysis (90°C, 3 months).

This substance is classified as a Class 1 Designated Chemical Substance under the PRTR Law. The main use of this substance is as a vulcanizing accelerator for chloroprene rubber, epichlorohydrin rubber, and chlorinated polyethylene. The production and import quantity for fiscal 2016 was not disclosed because the number of reporting businesses was not more than two. The production and import quantity in fiscal 2016 was more than 100 t.

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2. Exposure assessment

Total release to the environment in fiscal 2016 under the PRTR Law was 0.024 t (reported releases) . All reported releases were to the atmosphere. In addition, approximately 11 t was transferred to waste. The rubber product manufacturing industry reported large releases. A multi-media model used to predict the proportions distributed to individual media in the environment indicates that in regions where the largest quantities were estimated to have been released to the environment overall or the atmosphere in particular, the predicted proportion distributed to water bodies was 98.6%.

The maximum expected concentration of exposure to humans via inhalation could not be determined because general environmental atmospheric and indoor air survey data could not be obtained. The mean annual value for the atmospheric concentration in fiscal 2016 was calculated by use of a plume-puff model on the basis of releases to the atmosphere reported according to the PRTR Law; this model predicts a maximum level of 0.0064 μg/m^3.

Data for potable water, ground water, food and soil to assess oral exposure could not be obtained. Thereupon, assuming intake solely from public freshwater bodies, a maximum expected concentration of exposure of around less than 0.00072 μg/kg/day was obtained. River concentrations were not estimated because there were no releases to public water bodies reported in fiscal 2016 under the PRTR Law. The risk of exposure to this substance by intake from an environmental medium via food is considered slight, given its low bioaccumulation.

The predicted environmental concentration (PEC), which indicates exposure to aquatic organisms, was reported to be around less than 0.018 μg/L for both public freshwater bodies and seawater. There were no releases to public water bodies reported in fiscal 2016 according to the PRTR Law. On this account, river concentrations could not be calculated.

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3. Initial assessment of health risk

No information was available on acute symptoms in humans. Salivation and weight loss were observed in rats orally administered with this substance.

The carcinogenicity with a threshold value was suggested in some animal experiments. The threshold value is not definitive, but it is higher than the levels for which non-carcinogenic effects were observed. Therefore, the 'non-toxic level*' was identified on the basis of information on its non-carcinogenic effects assuming the existence of a threshold.

The LOAEL of 0.1 mg/kg/day for oral exposure (based on prolonged estrous cycle), determined from reproductive toxicity tests in rats, was divided by a factor of 10 to account for uncertainty in using a LOAEL. The calculated value of 0.01 mg/kg/day was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substance for oral exposure. The NOAEL for inhalation exposure of 11 mg/m^3 (based on increase in the thickness of the follicular epithelium, reduced colloid and hyperplasia in the thyroid, etc.), determined from toxicity tests in rats, was adjusted according to exposure conditions to obtain 2 mg/m^3 and subsequently divided by a factor of 10 to account for extrapolation to chronic exposure. The calculated value of 0.2 mg/m^3 was deemed to be the lowest reliable dose and was identified as the 'non-toxic level*' of the substance for inhalation exposure.

With regard to oral exposure, assuming the substance is absorbed via public freshwater bodies, the predicted maximum exposure level would be less than 0.00072 μg/kg/day, approximately. The MOE (Margin of Exposure) would exceed 280, when calculated from the predicted maximum exposure level and the 'non-toxic level*'of 0.01 mg/kg/day, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity in animals. Since exposure to the substance in environmental media via food is presumed to be limited, including it in the calculation would not change the MOE significantly. Therefore, no further work would be required at present to assess the health risk of this substance via oral exposure.

With regard to inhalation exposure, owing to the lack of identified exposure concentrations, the health risk could not be assessed. The maximum concentration (annual mean) in ambient air near the operators releasing large amount of the substance was estimated to be 0.0064 μg/m^3 based on the releases to air reported in FY 2016 under the PRTR Law. The MOE would be 630, when calculated from this concentration and the 'non-toxic level*' of 0.2 mg/m^3, and subsequently divided by a factor of 10 to account for extrapolation from animals to humans and by another factor of 5 to take into consideration the carcinogenicity in animals. Therefore, collection of further information would not be required to assess the health risk of this substance via inhalation in ambient air.

Toxicity				Exposure assessment		Result of risk assessment		Judgment
Exposure Path	Criteria for risk assessment	Animal	Criteria for diagnoses (endpoint)	Exposure medium	Predicted maximum exposure dose and concentration			
Oral	'Non-toxic level*' 0.01 mg/kg/day	Rats	Prolonged estrous cycle	Drinking water	- μg/kg/day	MOE	-	○
				Public freshwater bodies	<0.00072 μg/kg/day	MOE	>280	
Inhalation	'Non-toxic level*' 0.2 mg/m^3	Rats	Increase in the thickness of the follicular epithelium, reduced colloid and hyperplasia in the thyroid, etc.	Ambient air	- μg/m^3	MOE	-	○
				Indoor air	- μg/m^3	MOE	-	×

Non-toxic level *

- When a LOAEL is available, it is divided by 10 to obtain a NOAEL-equivalent level.
- When an adverse effect level for the short-term exposure is available, it is divided by 10 to obtain a level equivalent to an adverse effect level for the long-term exposure.

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4. Initial assessment of ecological risk

With regard to acute toxicity, the following reliable data were obtained: a 72-h EC_{50} exceeding 100,000 μg/L for growth inhibition in the green alga *Pseudokirchneriella subcapitata*, a 48-h EC_{50} of 13,300 μg/L for swimming inhibition in the

crustacean *Daphnia magna*, and a 96-h LC_{50} exceeding 1,000,000 μg/L for the fish species *Oryzias latipes* (medaka). Accordingly, based on these acute toxicity values and an assessment factor of 100, a predicted no effect concentration (PNEC) of 133 μg/L was obtained.

With regard to chronic toxicity, the following reliable data were obtained: a 21-d NOEC of 3,200 μg/L for reproductive inhibition in the crustacean *D. magna* and a 60-d NOEC of less than 100,000 μg/L for the fish species *Oncorhynchus mykiss* (rainbow trout). Accordingly, based on these chronic toxicity values and an assessment factor of 100, a PNEC of 32 μg/L was obtained.

The value of 32 μg/L obtained from the chronic toxicity to the crustacean was used as the PNEC for this substance.

The PEC/PNEC ratio was less than 0.0006 for both for freshwater bodies and seawater; accordingly, further work is considered unnecessary at this time.

Hazard assessment (basis for PNEC)			Assessment coefficient	Predicted no effect concentration PNEC (μg/L)	Exposure assessment		PEC/ PNEC ratio	Assessment result
Species	Acute/ chronic	Endpoint			Water body	Predicted environmental concentration PEC (μg/L)		
Crustacean *Daphnia magna*	Chronic	NOEC reproductive inhibition	100	32	Freshwater	<0.018	<0.0006	○
					Seawater	<0.018	<0.0006	

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5. Conclusions

	Conclusions		Judgment
Health risk	Oral exposure	No need for further work.	○
	Inhalation exposure	No need for further work.	○
Ecological risk	No need for further work.		○

［Risk judgments］ ○: No need for further work ▲: Requiring information collection

■: Candidates for further work ×: Impossibility of risk characterization

（▲）: Further efforts to collect data required based on comprehensive review of existing relevant data

（■）: Candidate for further work based on comprehensive review of existing data